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Practice-related effects demonstrate complementary roles of anterior cingulate and prefrontal cortices in attentional control☆

M.P. Milham,* M.T. Banich,¹ E.D. Claus,¹ and N.J. Cohen

The Beckman Institute, University of Illinois at Urbana-Champaign, 405 N. Matthews, Urbana, IL 61801, USA

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Abstract

The purpose of this study was to test the hypothesis that the dorsolateral prefrontal cortex (DLPFC), not the anterior cingulate cortex (ACC), plays the predominant role in implementing top-down attentional control. To do so, we used fMRI to examine practice-related changes in neural activity during a variant of the Stroop task. The results indicated that the DLPFC's activity decreased gradually as the need for control was reduced (as indexed by behavioral measures), while the ACC's activity dropped off rapidly. Such a pattern is consistent with the DLPFC taking a leading role in implementing top-down attentional control and the ACC being involved in other aspects of attentional control, such as response-related processes. In addition, with practice, there was a reduction in activity within cortical systems handling the processing of task-irrelevant information capable of interfering with task performance. This finding suggests that with practice the brain is capable of identifying and strategically inhibiting such processing.

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Introduction

While the advent of PET and fMRI rapidly advanced our ability to identify the network of neural structures involved in attentional control, the task of determining the respective contributions of these structures has proven to be far more challenging. Among the most controversial of topics is the determination of which region(s) implements attentional control (often referred to as *sources* of control; Frith et al., 2001). Despite general agreement that the frontal lobes are primarily responsible for implementing control, the relative contributions of specific regions such as the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex (ACC) are a continuing source of debate (Banich et al.,

2000a; Gehring and Knight, 2000; MacDonald et al., 2000; Milham et al., 2001; Pardo et al., 1990; Paus et al., 1993; Posner and DiGirolamo, 1998; Taylor et al., 1997).

The implementation of control involves: (1) modulation of neural activity within posterior processing regions in accord with task demands (i.e., amplifying neural activity within posterior processing systems handling task-relevant information while dampening that of posterior processing systems handling task-irrelevant information) and (2) the biasing of working memory processes such that the selection, maintenance, and manipulation of task-relevant representations is favored over that of task-irrelevant representations (see Milham et al., 2002, for a longer discussion of the neural mechanisms involved in these two processes).

Based on findings of increased ACC activity during tasks requiring response inhibition, selective attention, target selection, or novel responses, it has been suggested that the ACC is responsible for implementing attentional control (Bush et al., 1998; Peterson et al., 1999; Posner and Dehaene, 1994; Posner and DiGirolamo, 1998). However, reports of variability in ACC activity during the Stroop task, the gold standard of attentional selection tasks, cast doubt

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* Corresponding author. Fax: +1-217-244-8371.

E-mail address: mmilham@s.psych.uiuc.edu (M.P. Milham).

¹ Current address: Department of Psychology, University of Colorado at Boulder, E213-E Muenzinger Hall, 345 UCB, Boulder, CO 80309, USA.

on such a conclusion (Bench et al., 1993; Taylor et al., 1997). Furthermore, recent studies have found that when attentional demands are manipulated but response competition and/or response conflict is held constant, no modulation in the ACC's activity is noted (Banich et al., 2000b; Botvinick et al., 1999; Carter et al., 2000; MacDonald et al., 2000; Milham et al., 2001, 2002). In contrast, DLPFC's activity does vary with attentional demand. As we have noted (Milham et al., 2001), at a minimum, the failure to detect changes in the ACC's activity during manipulations of attentional selection when response-related factors are controlled restricts the situations under which the ACC can be posited to be responsible for implementing attentional control.

An alternative perspective that has emerged from this latter body of work posits that the DLPFC and the ACC play complementary roles in attentional control. Consistent with others, we have argued that the ACC is primarily involved in response-related processes (Paus, 1993; MacDonald et al., 2000; Milham et al., 2001; Paus, 2001), such as conflict monitoring (Carter et al., 1998, 2000; MacDonald et al., 2000), error detection (Gehring et al., 1993), and response facilitation/inhibition (Paus et al., 1993; Paus, 2001). In contrast, we have argued that the dorsolateral (BA 9 and BA 46) and posterior inferior PFC (BA 44) are responsible for the implementation of attentional control. Regions of the dorsolateral prefrontal cortex impose an "attentional set" for task-relevant information by modulating neural activity within posterior regions of the cortex responsible for processing such task-relevant information (e.g., V4 when color is the attribute to which an individual must respond) (for a similar perspective, see Carter et al., 2000; MacDonald et al., 2000). We have also argued that these regions facilitate the selection of task-relevant representations within working memory. To the degree that such top-down control is compromised, as in aged individuals, performance suffers and increases in activity are noted within both posterior processing regions that handle task-irrelevant information and inferior prefrontal regions involved in the maintenance of information within working memory (Banich et al., 2000a, 2000b; Milham et al., 2001, 2002).

It is important to note that while top-down control favors the activation of motor actions associated with task-relevant information, the activation of responses associated with task-irrelevant information is not necessarily abolished, especially when the processing of task-irrelevant information is relatively automatic. As such, even in the face of top-down control, some degree of facilitation and/or inhibition may be required at the level of response. We posit that these response processes are distinct from the top-down control imposed by the DLPFC and are supported by the ACC, a viewpoint consistent with others (e.g., Paus et al., 1993).

Here, we further test our hypothesis that the DLPFC and not the ACC plays the predominant role in top-down attentional control. Studies attempting to dissociate the DLPFC's and ACC's role in control typically compare patterns of neural activity across conditions with qualitative differences

either in the need for control or in how it is produced (e.g., response conflict vs. semantic conflict). In the present work, we took a different approach, comparing practice-related changes in the DLPFC's and ACC's activity during performance of an attentionally demanding Stroop-like interference task.

We felt that an examination of practice-related effects would be an effective means of testing if one of these regions (DLPFC, ACC) is more crucial to top-down attentional control than the other. Regions involved in implementing top-down control (i.e., imposing an attentional set for task-relevant information) should remain active as long as task-irrelevant information is a potent source of interference. Over the course of our experiment, the need for top-down control during our interference condition gradually decreased with practice, but was never abolished, as indexed by behavioral measures. A region involved in implementing such control should show a similar pattern of results—gradually decreasing, but showing some degree of sustained activity. Thus, we examined the impact of practice on the pattern of activity for the ACC and DLPFC separately to determine if one of the two areas exhibited a pattern of neural activity more consistent with a predominant role in implementing top-down control than the other. Although prior studies have demonstrated practice-related changes in the activity of the ACC and/or DLPFC for a variety of paradigms (e.g., verb-generation task, counting-word Stroop task, complex finger-tapping tasks) (e.g., Bush et al., 1998; Peterson et al., 1998), none have focused specifically on contrasting the relative impact of practice on these two brain areas during performance of a single task.

Our hypothesis that the DLPFC implements top-down attentional control whereas the ACC is involved in response-related processes predicts that with practice, the DLPFC's activity should be more sustained than that of the ACC. To test this prediction, we used a variant of the Stroop task introduced by MacLeod and Dunbar (1988) in which behavioral changes in attentional control can be observed over a relatively short period of time. We considered the standard Stroop paradigm ill-suited for the present investigation because it generally requires thousands of trials for significant practice effects to be observed behaviorally (MacLeod, 1991). In this modified Stroop paradigm, individuals were first taught to associate a unique color name to each of three previously unfamiliar shapes. Then we used fMRI to compare neural activity observed during blocks in which the shape's ink color (task-irrelevant dimension) conflicted with its name (*interference blocks*) with blocks in which it did not (i.e., the shape appeared in white) (*control blocks*). Practice-related effects were detected by identifying changes in the comparison of interference versus control blocks over time.

Our paradigm also enabled us to study the mechanisms by which the processing of task-irrelevant information is suppressed. Although models of attention typically posit that neural activity within processing systems containing

task-irrelevant information should be dampened, our prior neuroimaging work has demonstrated *increased* activity within these systems when the irrelevant information is related to the task-relevant dimension compared to when it is not. For example, when the task was to identify a word's ink color, increased activity was observed within word-processing regions when the word named a color (e.g., the word "red" in blue ink) compared to when it did not (e.g., the word "lot" in blue ink). Likewise, when the task was to identify an object's ink color, increased activity was observed within object-processing regions, when the object had a standard color with which it is associated (e.g., a frog is highly associated with the color green) compared to not (e.g., a car can be green but also red, blue, brown, tan, yellow, gray, white, black, and so forth) (Banich et al., 2000a, 2000b, 2001). We have speculated that this effect may occur for one of two reasons. First, it may be that top-down control is more "general," activating all regions processing information related to color rather than ink color specifically. This general tuning may be adaptive to avoid an initial "tunnel vision" regarding task-relevant information. With experience or practice, however, this tuning may become more refined. Another possibility is that activation spreads from brain regions that are processing task-relevant information. Thus, when V4 becomes activated, regions that process associated information about color may be primed. Regardless of which mechanism (or possibly both) accounts for activation in regions processing task-irrelevant information, we would expect that with practice top-down control should dampen activation in brain regions processing task-irrelevant information. The paradigm in the present study allows us to examine such a prediction.

In the current study, the item's ink color provides the task-irrelevant information that is related to the task-relevant dimension (i.e., the item's name that is a color). Thus, consistent with our prior studies, we predicted greater activity during interference blocks relative to control in those regions of the lingual and posterior fusiform gyri involved in color processing (Beauchamp et al., 1999; Corbetta et al., 1991; Zeki et al., 1991) at least early in task performance. However, these increases should be dampened over time, as participants become more experienced with selecting the shape's color name over the task-irrelevant ink color.

Methods

Stimuli

The stimuli consisted of three previously unfamiliar nonsense shapes.

Apparatus

All stimuli were programmed using Mel V2.0 and presented using an IBM-PC-compatible computer.

Training

Learning phase

Each of three previously unfamiliar nonsense shapes was shown in white along with one of three color words (i.e., "BLUE," "YELLOW," "GREEN") with which it was uniquely paired. Each shape–word pairing was viewed eight times outside the magnet, with the shape–word pairings occurring in a random order. Participants were instructed to learn to name each shape with the color word paired with it. At the end of this phase, we verified that participants could correctly provide the name for each of the three shapes with 100% accuracy.

Next, while obtaining anatomical scans, the shapes were presented in white without their associated color words, one at a time in a random order. The participants were instructed to practice naming each shape subvocally with its corresponding color word. Each shape was presented a total of 32 times.

Test phase

Stimuli/design. Our task made use of three ink colors: blue, yellow, and green. Two types of trials were included in the test phase: (1) *interference trials* in which the shape was printed in an ink color incongruent with the color used to name the shape and (2) *control trials* in which the shape was printed in white, which was not a color name for any of the shapes.

We made use of a blocked fMRI design (ABAB), in which control blocks were alternated with interference blocks. Participants were presented a total of six interference and six control blocks. Each block consisted of 18 trials, presented at a rate of one trial every 2 s. Each trial consisted of a 300-ms fixation cross followed by a 1200-ms presentation of the stimulus (shape) and a 500-ms inter-trial interval.

Procedure. Participants were instructed to subvocally name each shape with the corresponding color from the learning phase, while ignoring the ink color in which the shape was presented. Subvocalization was utilized in an effort to avoid possible motion artifacts. To obtain a measure of performance, participants were instructed to press a button at the point at which they started to respond subvocally. This measure was effective, as reliable slowing of reaction time was noted for interference relative to control trials (see "Behavioral results" section).

Data acquisition. A GE Signa (1.5 T) magnetic resonance imaging system equipped for echoplanar imaging (EPI) was used for data acquisition. Eleven right-handed native English-speaking participants (7 men 4 women; ranging in age from 18 to 30) were included in our study. For each run, a total of 300 EPI images were acquired (TR = 1517 ms, TE = 40 ms, flip angle 90°), each consisting of 15 contiguous slices (thickness 7 mm, in-plane resolution 3.75 mm), parallel to the AC-PC line. A high-resolution 3D anatomical set

(T1-weighted three-dimensional spoiled gradient echo images) was collected for each participant, as well as T1-weighted images of our functional acquisition slices. The head coil was fitted with a bite bar to minimize head motion during the session. Stimuli were presented on a goggle system designed by Magnetic Resonance Technologies.

Statistical analyses. Within-subject statistical analyses were carried out using FEAT, the FMRIB Easy Analysis Tool (<http://www.fmrib.ox.ac.uk/fsl/index.html>). The first seven volumes of each participant's time series were discarded to allow the MR signal to reach steady state. Prior to statistical tests, images were motion corrected using MCFLIRT (Jenkinson, 2001). The following prestatistics processing was applied: (1) spatial smoothing using a Gaussian kernel of FWHM 8 mm, (2) mean-based intensity normalization of all volumes by the same factor, (3) nonlinear high-pass temporal filtering (Gaussian-weighted LSF straight line fitting, with $\sigma = 54.0$ s), and (4) Gaussian low-pass temporal filtering HWHM 2.8 s.

Statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) (Woolrich, in submission). We modeled the difference between interference and control blocks separately for each third of the run, modeling the first two cycles, the second two cycles, and the last two cycles as independent conditions, to make the examination of practice effects possible. MedX 3.4 was used to transform parameter estimate (PE) maps for each contrast into a common stereotaxic space (Talairach and Tournoux, 1988). For each contrast, group random-effects analyses were used to test if the individual participants' PE values were reliably greater than 0.

Identification of regions of interest

The comparison of interference versus control trials during the first two cycles was used for identification of regions of interest for practice-related effects. Prior work in our laboratory has indicated that activations tend to be maximal during this period. Regions were defined as clusters of eight or more contiguous active voxels ($P < 0.0005$) (Forman et al., 1995). To limit the scope of our analyses to those regions relevant to the present work's goals (a priori regions of interest), we only included regions that have been identified in our prior studies of attentional control (Banich et al., 2000a, 2000b, 2001; Milham et al., 2001, 2002). These regions were those identified in the extrastriate and striate cortices (i.e., lateral occipital cortex, medial occipital cortex, fusiform gyrus), temporal cortex, posterior inferior and dorsolateral prefrontal cortices, and the medial walls of the frontal lobes. All regions of interest are reported in Table 2.

Region-based analysis

In this analysis, each of the ROIs was treated as a whole, to reduce variability associated with individual voxels. For

each region, we first calculated each participant's mean parameter estimate (beta) across voxels for each contrast. Next, the individual participants' mean parameter estimates for each region were entered into group random-effects analyses in which we tested if they were reliably nonzero.

Within-region analysis

Here we carried out a more fine-grained analysis that identified areas of maximal activation (i.e., peak activations) within our ROIs to ensure that their activity was not obscured in our region-based analysis by less active voxels. More specifically, using an automated peak detection algorithm outlined by Mintun et al. (1989), peak activations for the comparison of interference versus control were detected for the first two cycles, the second two cycles, and the third two cycles. Exploration was limited to voxels within our regions of interest.

For each unique peak identified, we defined a sphere (radius 2 voxels or 4 mm; total number of voxels in sphere 33), with the peak at its center. Next, for each sphere, the individual participants' mean parameter estimates for each pair of cycles were entered into group random-effects analyses in which we tested if they were reliably nonzero. It is important to note that we chose to report statistical scores for these spheres centered around maximally activated voxels rather than the individual voxels to be conservative and protect against noise associated with single voxels.

Results

Behavioral data

A repeated-measures ANOVA with the factors of Cycle (first two cycles, second two cycles, last two cycles) and Trial type (interference, control) yielded a main effect of Trial type ($F(1, 10) = 21.25, P < 0.001$), because responses were slower to interference than control trials, but no main effect of Cycle ($F(2, 20) = 0.118, P < 0.889$). A linear contrast [1 0 -1] of the interference effect across time (cycles 1 and 2, cycles 3 and 4, cycles 5 and 6) revealed a significant decrease in the magnitude of the interference effect from the first two cycles to the last two cycles ($F(1, 10) = 5.14, P < 0.047$) (see Fig. 1) (Control trials, cycles 1 and 2, 535 ms; cycles 3 and 4, 543 ms; cycles 5 and 6, 543 ms; Incongruent trials, cycles 1 and 2: 600 ms; cycles 3 and 4: 586 ms; cycles 5 and 6, 576 ms).

ACC, SMA, and DLPFC

Consistent with prior studies of the Stroop task, the comparison of interference and control blocks during the first two cycles revealed an extensive pattern of activity throughout the ACC, pre-SMA, and DLPFC (see Fig. 2 and Tables 1 and 2). While these regions all showed practice-

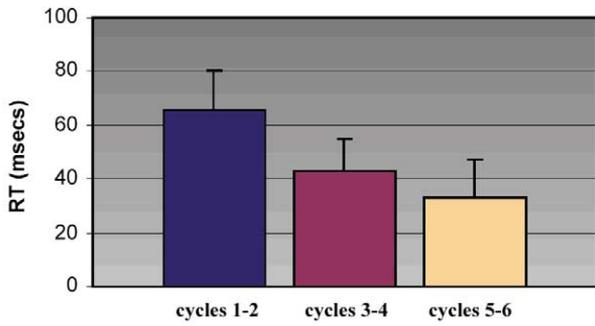


Fig. 1. Behavioral data. A significant interference effect (interference – control) was noted. Contrasts revealed a significant linear decrease in the magnitude of the interference effect as a function of cycle ($P < 0.047$)

related decreases in activity, of most importance to our hypotheses, the regions differed with respect to the time course and extent of practice-related decreases observed. Consistent with our assertion that the ACC does not play a predominant role in implementing control, both region-based and within-region analyses found that significant activity within the ACC/pre-SMA dropped off quickly, being limited to the first two cycles. In contrast, significant activations within regions of the left middle frontal gyrus and left posterior inferior frontal gyrus were more sustained, occurring across the first four cycles (see Fig. 2) and tending toward significant activity for the last two cycles (e.g., Table 1, BA 9, $x = -42, y = 30, z = 30, P < 0.06$). This activation for the last two cycles probably failed to reach significance because of increasing variability across participants.

To verify the rapid drop-off of activity within medial wall regions, we tested the contrast representing the cycle \times condition interaction ([1 -0.5 -0.5]). We obtained significant values for each of the medial wall regions as a whole (BA 32, $P < 0.03$; BA 9/32, $P < 0.025$; BA 6, $P < 0.006$), as well as local peaks within the regions (range of significance values for peaks, $P < 0.02$ – 0.0005). It is also important to note that our failure to detect ACC/pre-SMA activity during later cycles does not appear to be a power-related issue, because peaks within this region showed trends toward decreased activity during interference blocks (see Fig. 2). Such a pattern for the ACC is clearly inconsistent with a role in the implementation of attentional control.

Finally, we carried out an analysis to provide a direct comparison of the impact of experience with selection on activation of the DLPFC and medial wall regions. More specifically, we directly compared the percentage of reduction in neural activity (based on parameter estimates) from the first two cycles to the later cycles (3 and 4, 5 and 6) for peaks in each of the two regions (i.e., the DLPFC, the ACC/pre-SMA) (see Fig. 3). To be conservative, the data from one subject were excluded from this analysis. His parameter estimate for the first two cycles was slightly negative (cycles 1 and 2, -3; cycles 3 and 4, 11; cycles 5 and 6, 4), indicating that unlike all the other participants he did not exhibit any activation in the DLPFC. Inclusion of this participant would have erroneously decreased the percentage reduction for the DLPFC because his value for this region was more than 3 SD less than the mean. Because inclusion of his data would have biased our results in favor

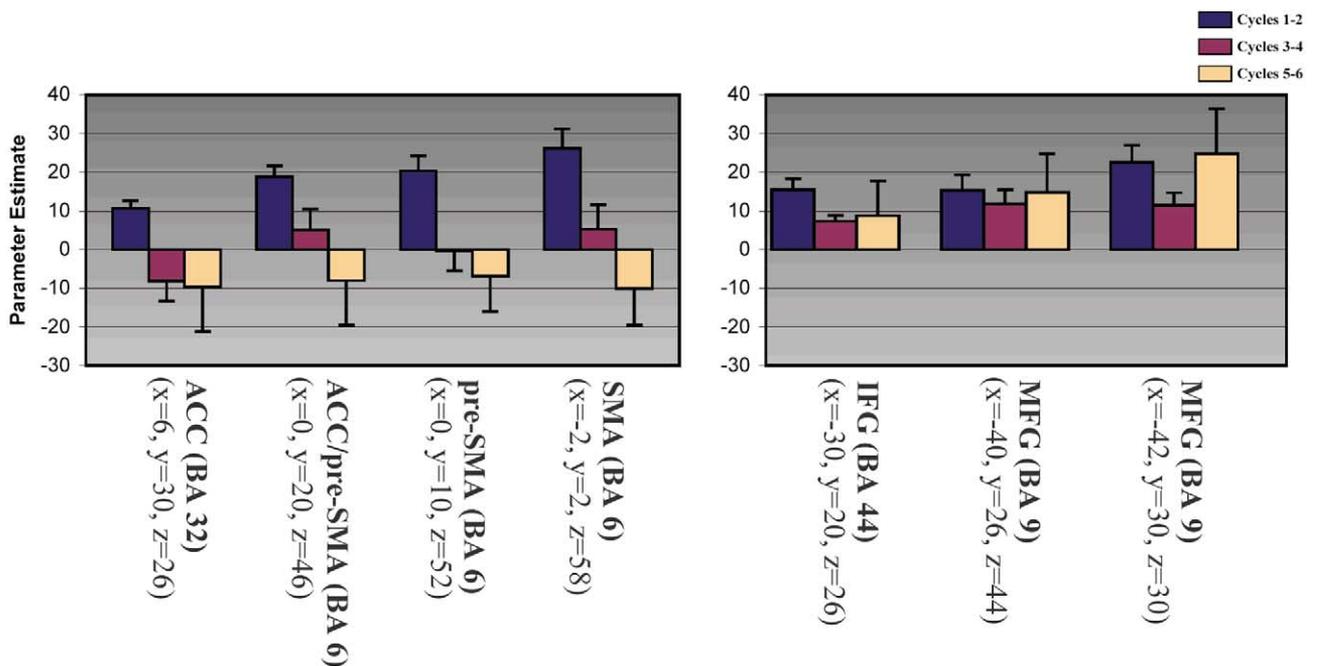


Fig. 2. Interference versus control. Practice-related decreases in the ACC’s activity were more rapid and pronounced than those in DLPFC. The more sustained activity noted in DLPFC is consistent with its proposed role in the implementation of attentional control. (Left) Medial wall; (right) L. DLPFC and PIPFC.

Table 1
Within-region analysis

Region	BA	Peaks			-logProb		
		x	y	z	Cycles 1 and 2	Cycles 3 and 4	Cycles 5 and 6
Fusiform gyrus	19	-32	-70	-12	3.5	2.7	(-)1.3
Fusiform gyrus	37	48	-54	-14	3.5	1.4	NS
Fusiform gyrus	19	28	-50	-10	3.4	1.8	NS
Fusiform gyrus	19	38	-70	-4	7	NS	NS
Fusiform gyrus	19/37	-34	-62	-8	3.3	3.6	NS
Lateral occipital cortex							
Inferior occipital gyrus	21/37	32	-78	-2	5.6	1.2	NS
Middle occipital gyrus	19	-26	-78	8	3	3.3	NS
Orbital gyrus	18/19	-34	-80	2	4.4	3	NS
Middle occipital gyrus	19	-40	-80	10	4.1	NS	NS
Middle occipital gyrus	19	-24	-88	18	5	NS	NS
Medial occipital cortex							
Cuneus	17	8	-86	10	4.3	NS	(-)1.6
Lingual gyrus	18	14	-74	-6	3.1	NS	(-)1.4
Temporal cortex							
Superior temporal gyrus	22	52	-26	2	4.7	2.5	NS
Inferior temporal gyrus	37	58	-56	-6	5.6	1.5	(-)1.3
Inferior temporal gyrus	37	-46	-54	-4	4.6	1.5	NS
Middle temporal gyrus	21/37	62	-50	-2	4.6	1.3	NS
Middle temporal gyrus	37	-44	-54	4	4	NS	NS
Middle temporal gyrus	19	40	-72	18	4	NS	NS
Middle temporal gyrus	21	48	-40	-8	3.3	NS	NS
Medial wall							
Medial frontal gyrus	6	-2	2	58	3.4	NS	NS
Cingulate gyrus	32	6	30	26	3.4	NS	NS
Medial frontal gyrus	8	2	30	36	3.2	NS	NS
Medial frontal gyrus	6	0	20	46	4.3	NS	NS
Superior frontal gyrus	6	0	10	52	3.4	NS	NS
DLPFC and PIPFC							
Middle frontal gyrus	9	-42	30	30	3.4	2.3	1.2
Middle frontal gyrus	8	-40	26	44	2.5	2.1	NS
Inferior frontal gyrus	44	-30	20	26	3.6	3.3	NS
Middle frontal gyrus	9	38	46	34	3.3	NS	NS

Note. $-\log(0.050) = 1.301$; $-\log(0.005) = 2.301$; $-\log(0.0005) = 3.301$.

(-), deactivation.

of dissociating activity in the DLPFC and ACC/pre-SMA, we excluded him to provide a strong test of our hypothesis. Using a paired comparison across participants to examine the percentage of reduction in activity for these brain areas, we found a significantly greater reduction of the medial wall during cycles 3 and 4 than of the DLPFC ($P < 0.037$). This provides direct evidence of a more rapid drop-off in activity of medial wall regions than the DLPFC, consistent with our predictions. By cycles 5 and 6, the reduction in neural activity for medial wall regions was still greater than for the DLPFC, but only marginally so ($P < 0.075$).

Consistent with the assertion that decreases in DLPFC activity reflect decreases in the need for attentional control, a correlation analysis revealed that those subjects showing a greater drop-off in the interference effect (interference minus control RT) from cycles 1 and 2 to cycles 3 and 4 showed a greater percentage of reduction in DLPFC activity during cycles 3 and 4 (relative to cycles 1 and 2) ($r = 0.584$; $P < 0.038$).

It is important to note that our analyses took into account

several methodological concerns that could provide alternative explanations for our finding that practice differentially impacts the ACC and DLPFC. First, one may be concerned that the differential impact of practice on the ACC and DLPFC could be attributed to differences in the sizes of the regions, because smaller regions are more likely to show homogeneous activity. With regard to this concern about the impact of a region's size or shape on the observed practice effect, we draw attention to our within-region analyses (Table 1), which were described in detail under Methods. In contrast to our region-based analyses that examined neural activity at the cluster level (the size of which can vary from region to region), our within-region analyses reported statistics for spheres (fixed in size, diameter 5 voxels) centered around peak activations within each region. Such an analysis is not impacted by a region's size or shape. The data shown in Table 1 and Figs. 2 and 3, which were based on these spheres centered around peak activations, not the clusters, clearly show a differential impact of practice on the ACC and DLPFC.

Table 2
Region-based analysis

Region	BA	COI			-logProb		
		x	y	z	Cycles 1 and 2	Cycles 3 and 4	Cycles 5 and 6
Fusiform gyrus	19	28	-50	-10	3.9	1.6	NS
Fusiform gyrus	19	-22	-48	-10	4.7	NS	NS
Lateral occipital cortex							
Middle occipital gyrus	19/37	-34	-74	4	7.2	2.4	NS
Middle occipital gyrus	19	42	-66	-4	7.4	1.6	NS
Medial occipital cortex							
Lingual gyrus	18/19	14	-74	-4	3.5	NS	(-)1.9
Lingual gyrus	18	8	-86	10	4.8	NS	(-)1.8
Temporal cortex							
Superior temporal gyrus	22	52	-28	4	5.3	1.4	NS
Middle temporal gyrus	19	38	-72	18	5	NS	NS
Medial wall							
Cingulate gyrus	32	6	28	26	3.9	NS	NS
Cingulate gyrus	32/9	2	30	36	4	NS	NS
Superior frontal gyrus	6	16	4	60	4.6	NS	NS
Middle frontal gyrus	6	-2	12	52	5.1	NS	NS
DLPFC and PIPFC							
Middle frontal gyrus	9	42	16	40	6.2	NS	NS
Middle frontal gyrus	9	-40	16	32	6.3	1.6	NS
Middle frontal gyrus	46	-52	26	24	3.7	NS	NS
Middle frontal gyrus	8/9	-48	26	42	4	NS	NS
Middle frontal gyrus	8	-36	24	48	4.3	NS	NS

Note. $-\log(0.050) = 1.301$; $-\log(0.005) = 2.301$; $-\log(0.0005) = 3.301$.

(-), deactivation.

Another possible concern is that ACC and DLPFC regions may be differentially impacted by noise. While a valid concern, we draw attention to the fact that the effect size noted within the ACC during cycles 1 and 2 was similar to, if not greater than, that observed in the DLPFC (see Fig. 2). As such, we do not believe that there should be concern about our ability to detect activity within the ACC relative to the DLPFC, because we were clearly able to detect both ACC and DLPFC activity during the first cycles. Furthermore, our analysis depicted in Fig. 3 attempts to remove any baseline differences in the magnitude of the signal detected

in the two regions by looking at the percentage of reduction in signal over time, rather than just the magnitude of reduction. Additionally, there is no reason to expect a decrease in the ability to detect activity within one region as opposed to the other as a function of time.

An additional concern might be that the differential impact of practice on the ACC and DLPFC could be explained by regression toward the mean. More specifically, one may question if the differential impact of practice could be explained by differences in the size of the initial change observed in each region, because regression toward the mean would predict greater reductions in regions with larger initial changes. We doubt that this can explain the pattern of our data for several reasons. First, as is reflected in Fig. 2, the peak within the medial wall with the smallest increase in activity during cycles 1 and 2 demonstrated the most rapid drop-off in activity—a finding that directly contradicts the idea that the regions with largest initial change will show the greatest subsequent drop-off. Furthermore, looking across the regions in Fig. 2, there is no evidence that peaks with larger initial responses showed the most rapid drop-off, as can be seen by comparing the data for the third peak listed within the DLPFC with the second or third listed in the medial wall. Also, if regression toward the mean explained the pattern of our data, the response of the DLPFC should drop continuously from one cycle to the next. However, as is evident from Fig. 2, peaks within the DLPFC maintained neural activity and/or showed rebound increases

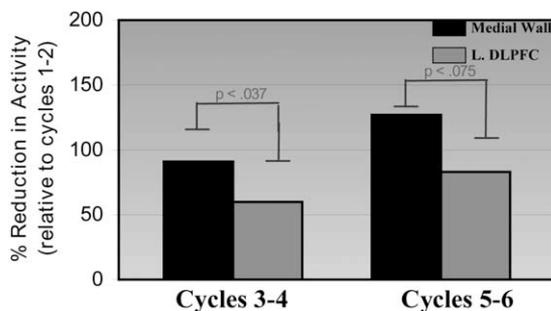


Fig. 3. Differential impact of practice on the left DLPFC and the medial wall activity. Consistent with our prediction that ACC activity should drop off more rapidly than DLPFC activity, a paired *t* test revealed a significantly greater reduction in medial wall activity than L.DLPFC activity during cycles 3 and 4. For cycles 5 and 6, the differential reduction in neural activity for the ACC and L. DLPFC was marginally significant.

for some participants during the last two cycles—a pattern that clearly cannot be explained by regression toward the mean. Finally, in our analysis that directly compared the drop-off in activity between the DLPFC and the ACC, we used the percentage of reduction in activity to help take into account differences with respect to the initial change observed within a region.

Thus, across all of our different analyses, we provided clear evidence of a more sustained involvement of the DLPFC in attentional control over the course of task performance. This is consistent with the notion that the DLPFC is involved in the implementation of attentional control, while medial wall regions are not.

Extrastriate and striate cortex

Several practice-related changes in activity were noted within the occipital cortex, providing insights into attentional modulation of task-relevant and task-irrelevant processing systems. First, given that ink color was the task-irrelevant attribute in the current experiment, we examined patterns of neural activity (interference > control) within regions of the medial occipital cortex previously identified as color-sensitive (e.g., V4) (Corbetta et al., 1991; Zeki et al., 1991; Clark et al., 1997; Beauchamp, 1999). Both the region-based and the within-region analyses indicated that activity on interference compared to control blocks was limited to the first two cycles. Furthermore, these same regions as well as the posterior portion of the left fusiform gyrus, another region thought to be involved in color processing (Beauchamp et al., 1999), exhibited significant deactivations during the last two cycles (see Tables 1 and 2). It should be noted that the area of the lingual gyrus in which these deactivations were noted ($x = 14, y = -74, z = -6$) is similar to regions identified by PET and fMRI as involved in color perception and attention to color (within 8 mm of that noted by Clark et al. (1997); within 9 mm of that noted by Corbetta et al. (1991); within 12 mm of that noted by Zeki et al. (1991). In sum, regions handling task-irrelevant information related to the task at hand (i.e., color information) initially exhibited increased activation, but then with practice, actually exhibited deactivations.

It appears that neural activity within the task-irrelevant processing system initially increases during conditions of conflict, similar to findings in our prior studies (e.g., Banich et al., 2000a, 2001), but then is dampened as the brain becomes more experienced with the selection of task-relevant information over task-irrelevant information. Interestingly, during the third pair of cycles, activity within the posterior portion of the DLPFC (BA 8) was positively correlated with that noted in the lingual gyrus ($r = 0.78, P < 0.005$). This correlation indicates that for a given participant, less activity within the task-irrelevant processing system is associated with a decreased need for top-down control, as indexed by activity within the posterior DLPFC during interference relative to control blocks. In the discus-

sion we provide a more detailed consideration of DLPFC/extrastriate interactions.

In contrast to the regions responsible for processing color (task-irrelevant information), regions thought to handle the task-relevant information about the shape's form (e.g., Kelley et al., 1998) exhibited more sustained increases in neural activity, extending into the second two cycles. More specifically, sustained increases in activity were noted within the lateral occipital cortex, the anterior fusiform gyrus, and portions of temporal cortex. These increases in activity probably reflect an amplification of neural activity within task-relevant processing systems (i.e., regions involved in the encoding of the object's form), consistent with many other neuroimaging studies (e.g., Corbetta et al., 1991). Similar to the DLPFC, activity within these regions during interference blocks retreats to that observed for control blocks during the last two cycles.

Discussion

Examination of practice-related changes in neural activity provided clear evidence of the differential involvement of the ACC and DLPFC in attentional control; practice-related decreases in the ACC's activity were more rapid and more pronounced than those in the DLPFC. Findings of such a rapid drop-off in ACC activity (during cycles 3–6) despite the continued need for maintenance of an attentional set (as indicated by the presence of a behavioral Stroop interference effect) are not consistent with models proposing a role for the ACC in implementing attentional control (Bush et al., 1998; Peterson et al., 1999; Posner and Dehaene, 1994; Posner and DiGirolamo, 1998; Posner et al., 1988). Our finding that some ACC subregions exhibited trends toward an actual decrease in activity on interference relative to control trials in later cycles is especially inconsistent with such a role. In contrast, the more sustained activity noted in the DLPFC is consistent with models positing that the DLPFC is primarily responsible for the implementation of top-down attentional control (Banich et al., 2000a, 2000b; MacDonald et al., 2000; Milham et al., 2001, 2002; Miller and Cohen, 2001).

The rapid drop-off of ACC activity is consistent with a role of the ACC in response-related processes, as suggested by our laboratory and others (Banich et al., 2000b; Carter et al., 2000; MacDonald et al., 2000; Milham et al., 2001; Paus, 2001; Van Veen et al., 2001). Prior studies have shown that the degree of conflict experienced at the level of response decreases as the degree of attentional control increases (Carter et al., 2000). In our study, less ACC activity was observed as the implementation of attentional control became more effective (as reflected by a decrease in the behavioral Stroop interference effect). This finding suggests that with practice, the need for control is limited to earlier, nonresponse levels of processing.

One concern that some may have concerning our find-

ings is that they can be viewed as supportive of the presence of quantitative rather than qualitative differences between the lateral and medial prefrontal cortex. In other words, our data may show differences in the degree to which the lateral and medial frontal cortex are involved in control rather than differences in the nature of their contributions. In considering the validity of this concern, it is important to note that our data provide quantitative evidence of a proposed qualitative difference in the DLPFC's and ACC's respective roles in control—namely that the DLPFC is involved in implementing control and the ACC is involved in response-related processes. Based on our hypothesis, we predicted that the patterns of activity for these two regions should differ with respect to the impact of practice, with the DLPFC showing a pattern more consistent with a role in implementing control. Our findings verified our hypothesis' prediction. So, while it may be argued that we have only demonstrated a quantitative difference in patterns of neural activity for the two regions, it is important to note that the presence of this quantitative difference supports the proposed qualitative difference between the lateral and medial prefrontal cortex's contributions to attentional control.

The current results have implications for two prominent theories of ACC function. One posits that the ACC plays an important role in conflict monitoring (Carter et al., 1998; Cohen et al., 2000; MacDonald et al., 2000). When conflict is detected, this theory posits that the ACC signals the DLPFC to increase its activity, thereby enhancing the degree of top-down control. In contrast, others suggest that the ACC is primarily responsible for conflict resolution at the response level, not conflict monitoring (Paus, 2001). Taken at face value, our findings appear to be inconsistent with the notion put forth by the conflict-monitoring hypothesis that the involvement of the DLPFC in attentional control is linked to the ACC's ability to detect conflict (e.g., Cohen et al., 2000), because we found increases in DLPFC activity to be somewhat independent of the ACC's activity. However, our data do not preclude a modified version of the conflict-monitoring hypothesis. It may be that conflict monitoring by the ACC is *initially* needed to recruit top-down control by the DLPFC, but not to maintain DLPFC's continued engagement in control. Such a suggestion is consistent with our findings that ACC activity was only noted early on in task performance (cycles 1 and 2).

However, we think that a more parsimonious explanation of our data is the viewpoint that we have posited previously, which is that the ACC primarily provides feedback to the DLPFC concerning the occurrence of conflict at the response level (Milham et al., 2001). When conflict arises at nonresponse levels, the DLPFC possesses other means of detecting the need for its involvement in control, independent of the ACC, most likely through its own bidirectional connections with posterior processing regions (see Petrides, 2000, for a discussion of these connections). Thus, the DLPFC can become active independent of the ACC. But when conflict is detected at the response level, the ACC acts

to further increase top-down control by the DLPFC, thereby reducing the potential for an erroneous response. These ideas are discussed further in other papers (Milham, et al., 2002; Milham et al., in submission; Milham, unpublished doctoral dissertation).

The present study also provided new insights into attentional modulation of neural activity within the systems that process task-relevant and task-irrelevant information. Consistent with the predictions of most models of attention, increases in activity were noted in regions involved in processing the task-relevant information, the object's form (i.e., lateral occipital and anterior fusiform cortex) (Kelley et al., 1998). However, early on (cycles 1 and 2), we also found increased neural activity within the task-irrelevant processing system (i.e., lingual gyrus and posterior fusiform gyrus) increased during interference blocks, a finding consistent with many of our prior studies (Banich et al., 2000a, 2000b, 2001).

At first glance such findings may appear paradoxical, as most models of attention would generally argue for a strategic dampening of processing associated with task-irrelevant information. However, we noted in the past that these activations did appear more limited, at least with regard to spatial extent, when compared with those observed when the same attribute is task-relevant. For example, in a study of the color-object Stroop task (Banich et al., 2000a), in which we compared activation for items viewed in atypical colors (e.g., a red frog) with items shown in one of their many possible colors (e.g., a red car), activations were noted throughout the ventral processing stream. However, they did not extend as far anterior as those noted in studies of object encoding (Kelley et al., 1998). Also, in a recent study in which we compared patterns of neural activity in older (ages 65 and over) and younger adults during the color-word Stroop task, we found that for older adults, in whom the DLPFC is less responsive and attentional control is less effective, increases in neural activity extended further along the ventral visual processing stream than those in young adults (Milham et al., 2002).

The present study, however, provides the clearest picture of attentional modulation in task-irrelevant processing systems. These seemingly paradoxical increases in activity within the task-irrelevant processing system diminished with experience and were actually replaced by deactivations during interference blocks in later cycles of our task (cycles 5 and 6). These data clearly suggest that as the brain becomes experienced with the selection of task-relevant over task-irrelevant information, neural activity within the processing system(s) handling task-irrelevant information is strategically inhibited. It is also important to note that participants who exhibited greater decreases in activity within the brain region responsible for processing task-irrelevant information showed less activity within the posterior DLPFC during incongruent blocks in the final two cycles. This association is consistent with the notion that the DLPFC responds to the need for control created by inter-

ference from the outputs of task-irrelevant processing systems.

An important question raised by these findings concerns why activity within regions processing task-irrelevant information should increase, at least initially. One possibility is that when two or more processing systems introduce conflicting representations into working memory, anterior regions (i.e., the DLPFC) may actually amplify neural activity within each processing system, before selecting the correct, task-relevant representation. Such a process would provide a better “look” at each representation before selecting the one that is most task-relevant. Given that the same processing system is selected trial after trial, experience may allow the brain to fine-tune its strategy, limiting amplification of neural activity to the task-relevant processing system and actually inhibiting neural activity within the task-irrelevant processing system. Alternatively, it is possible that because our response set consists of color words, the concept of color is primed each time the participant generates a response. As such, the semantic and perceptual representations associated with the incongruent ink colors are primed, thereby enabling these task-irrelevant representations to achieve a higher level of activity and become more potent sources of interference (see MacLeod, 1991, for further discussion of this concept). With practice, such activity is dampened in an effort to reduce the ability of such task-irrelevant representations to produce conflict. This issue will require further examination to provide a definitive answer (see Banich et al., 2001, for other possible mechanisms).

A final explanation of our data that we consider (and then discount) is that a new and different set of brain regions becomes important for top-down attentional control with practice. We have argued that even by the end of our experiment, the DLPFC maintains some degree of involvement in control, although obviously much decreased. However, it remains logically possible that with a higher degree of practice some other brain region may begin to take a more prominent role in top-down control. Other studies of changes in patterns of brain activation with practice have found that different subsystems may become engaged as practice with the task increases. For example, in a study of practice-related changes in neural activity in the verb-generation task, Petersen et al. (1998) found that practice produced a switch from activity in control regions (i.e., ACC, DLPFC) to activity in a network of structures thought to carry out more automated routines (i.e., insular cortex). To investigate this possibility, we looked at the voxelwise scores for the comparison of interference versus control for cycles 5 and 6 across all voxels. At a level of $P < 0.005$, we only found significant voxels (clusters of 3–5 voxels) in the DLPFC and superior parietal cortex. This pattern suggests some degree of continued involvement of the same control structures, though much dampened, rather than recruitment of a different set of structures.

In summary, the present study had two significant findings. First, it provides clear evidence for the dissociation of

the DLPFC and ACC in attentional control, with the DLPFC and not ACC being implicated in the implementation of top-down attention control. Second, it demonstrates that with experience, the brain is capable of identifying and strategically inhibiting cortical systems handling the processing of task-irrelevant information capable of interfering with task performance.

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